

Please type a plus sign (+) inside this box →



PTO/SB/08A (10-96)
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT



(Use as many sheets as necessary)

Page 1 of 6

Complete if Known

Application Number	09/506,988
Filing Date	February 18, 2000
First Named Inventor	Jordan J.N. Tang
Group Art Unit	1614
Examiner Name	
Attorney Docket Number	OMRF 176

OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
JN		BALDWIN, et al., "Structural basis of drug resistance for the V82A mutant of HIV-1 proteinase," <i>Nat. Struct. Biol.</i> 2(3):244-9 (1995).	
		BOGER, "Renin Inhibitors. Design of Angiotensinogen Transition-state Analogs Containing Statine: Conformationally restricted inhibitors and a model for the bound conformation of renin substrate," in <i>Aspartic Proteinases and Their Inhibitors</i> , (Kostka, V., ed.), pp. 401-420, Walter de Gruyter: N.Y., 1985.	
		CARPENTER, et al., "Antiretroviral therapy for HIV infection in 1998: Updated recommendations of the International AIDS Society-USA Panel," <i>JAMA</i> 280(1):78-86 (1998).	
		CARROLL, et al., "Identification of potent inhibitors of <i>Plasmodium falciparum</i> plasmepsin II from an encoded statine combinatorial library," <i>Bioorg. Med. Chem. Lett.</i> 8(17):2315-20 (1998).	
		CARROLL, et al., "Evaluation of a structure-based statine cyclic diamino amide encoded combinatorial library against plasmepsin II and cathepsin D," <i>Bioorg. Med. Chem. Lett.</i> 8(22):3203-6 (1998).	
		CHEN, et al., "Three-dimensional structure of a mutant HIV-1 protease displaying cross-resistance to all protease inhibitors in clinical trials," <i>J. Biol. Chem.</i> 270(37):21433-6 (1995).	
		COFFIN, "HIV population dynamics in vivo: implications for genetic variation, pathogenesis, and therapy," <i>Science</i> 267(5197):483-9 (1995).	
		CONDRA, et al., "Genetic correlates of in vivo viral resistance to indinavir, a human immunodeficiency virus type 1 protease inhibitor," <i>J. Virol.</i> 70(12):8270-6 (1996).	
		CONDRA, et al., "In vivo emergence of HIV-1 variants resistant to multiple protease inhibitors," <i>Nature</i> 374(6522):569-71 (1995).	
		CRAIG, et al., "Antiviral properties of Ro 31-8959, an inhibitor of human immunodeficiency virus (HIV) proteinase," <i>Antiviral Res.</i> 16(4):295-305 (1991).	

Examiner's Signature

JM

Date Considered

7 Sept 2000

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →



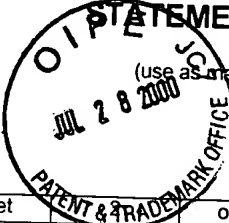
PTO/SB/08A (10-96)
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)



Sheet 1 of 6

Complete if Known

Application Number	09/506,988
Filing Date	February 18, 2000
First Named Inventor	Jordan J.N. Tang
Group Art Unit	1614
Examiner Name	
Attorney Docket Number	OMRF 176

OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
mm		DEBOUCK & METCALF, "Human Immunodeficiency Virus Protease: A target for AIDS therapy," <i>Drug Devel. Res.</i> 21:1-17 (1990).	
		DEBOUCK, et al., "Human immunodeficiency virus protease expressed in <i>Escherichia coli</i> exhibits autoprocessing and specific maturation of the gag precursor," <i>Proc. Natl. Acad. Sci. USA</i> 84:8903-8907 (1987).	
		DORSEY, et al., "L-735,524: the design of a potent and orally bioavailable HIV protease inhibitor," <i>J. Med. Chem.</i> 37(21):3443-51 (1994).	
		DUNN, et al., "Subsite preferences of retroviral proteinases," <i>Methods Enzymol.</i> 241:254-178 (1994).	
		ERMOLIEFF, et al., "Kinetic properties of saquinavir-resistant mutants of human immunodeficiency virus type 1 protease and their implications in drug resistance <i>in Vivo</i> ," <i>Biochemistry</i> 36(40):12364-70 (1997).	
		GHOSH, et al., "3-tetrahydrofuran and pyran urethanes as high-affinity P ₂ -ligands for HIV-1 protease inhibitors," <i>J. Med. Chem.</i> 36:292-94 (1993).	
		GHOSH, et al., "An efficient synthesis of hydroxyethylene dipeptide isosteres: The core unit of potent HIV-1 protease inhibitors," <i>J. Org. Chem.</i> 56:6500-3 (1991)	
		GRAVES, "Human immunodeficiency virus proteinase: now, then, what's next?" <i>Adv Exp Med Biol.</i> 306:395-405 (1991).	
		GULNIK, et al., "Kinetic characterization and cross-resistance patterns of HIV-1 protease mutants selected under drug pressure," <i>Biochemistry</i> 34(29):9282-7 (1995).	
my		HO, et al., "Rapid turnover of plasma virions and CD4 lymphocytes in HIV-1 infection," <i>Nature</i> 373(6510):123-6 (1995).	

Examiner's Signature

gmfeaver

Date Considered

7 Sept 2000

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

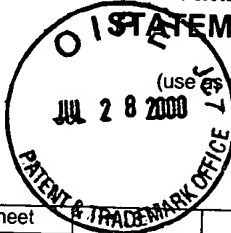
Please type a plus sign (+) inside this box →





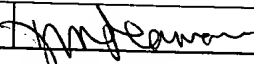
PTO/SB/08A (10-96)
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

+

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) 		Application Number	09/506,988
		Filing Date	February 18, 2000
		First Named Inventor	Jordan J.N. Tang
		Group Art Unit	1614
		Examiner Name	
		Attorney Docket Number	OMRF 176
Sheet	of	6	

OTHER ART - NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
		DUNN, et al., "Subsite Preferences of Retroviral Proteinases" <i>Methods in Enzymology</i> 241:254-278 (1994).	
		HONG, et al., "Active-site mobility in human immunodeficiency virus, type 1, protease as demonstrated by crystal structure of A28S mutant," <i>Protein Sci.</i> 7(2):300-5 (1998).	
		HONG, et al., "Crystal structures of complexes of a peptidic inhibitor with wild-type and two mutant HIV-1 proteases," <i>Biochemistry</i> 35:123-126 (1996).	
		HOOVER, et al., "Discovery of inhibitors of human renin with high oral bioavailability," <i>Adv Exp Med Biol.</i> 362:167-80 (1995).	
		IDO, et al., "Kinetic studies of human immunodeficiency virus type 1 protease and its active-site hydrogen bond mutant A28S," <i>J. Biol. Chem.</i> 266(36):24359-66 (1991).	
		JACOBSEN, et al., "Characterization of human immunodeficiency virus type 1 mutants with decreased sensitivity to proteinase inhibitor Ro 31-8959," <i>Virology</i> 206(1):527-34 (1995).	
		JACOBSEN, et al., "In vivo resistance to a human immunodeficiency virus type 1 proteinase inhibitor: mutations, kinetics, and frequencies," <i>J. Infect. Dis.</i> 173(6):1379-87 (1996).	
		KEMPF, et al., "ABT-538 is a potent inhibitor of human immunodeficiency virus protease and has high oral bioavailability in humans," <i>Proc. Natl. Acad. Sci. U S A.</i> 92(7):2484-8 (1995).	
		KOHL, et al., "Active human immunodeficiency virus protease is required for viral infectivity," <i>Proc. Natl. Acad. Sci. USA</i> 85(13):4686-90 (1988).	
		LAPATTO, et al., "X-ray analysis of HIV-1 proteinase at 2.7 Å resolution confirms structural homology among retroviral enzymes," <i>Nature</i> 342(6247):299-302 (1989).	

Examiner's Signature		Date Considered	7 Sept 00
----------------------	---	-----------------	-----------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

+

Please type a plus sign (+) inside this box →



PTO/SB/08A (10-96)
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

+

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)		Application Number	09/506,988
		Filing Date	February 18, 2000
		First Named Inventor	Jordan J.N. Tang
		Group Art Unit	1614
		Examiner Name	
		Attorney Docket Number	OMRF 176
Sheet	of	6	

OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
ms		LIN, et al., "Effect of point mutations on the kinetics and the inhibition of human immunodeficiency type 1 protease: Relationship to drug resistance," <i>Biochemistry</i> 34:1143-1152 (1995).	
		MAJER, et al., "Structure-based subsite specificity mapping of human cathepsin D using statine-based inhibitors," <i>Protein Sci.</i> 6(7):1458-66 (1997).	
		MARCINISZYN, et al., "Mode of inhibition of acid proteases by pepstatin," <i>J. Biol. Chem.</i> 251(22):7088-94 (1976).	
		MELLORS, "Closing in on human immunodeficiency virus-1," <i>Nat. Med.</i> 2(3):274-5 (1996).	
		MOLLA, et al., "Ordered accumulation of mutations in HIV protease confers resistance to ritonavir," <i>Nat. Med.</i> 2(7):760-6 (1996).	
		MULICHAK & WATENPAUGH, "The crystallographic structure of the protease from human immunodeficiency virus type 2 with two synthetic peptidic transition state analog inhibitors," <i>J. Biol. Chem.</i> 268(18):13103-9 (1993).	
		NAVIA, et al., "Three-dimensional structure of aspartyl protease from human immunodeficiency virus HIV-1," <i>Nature</i> 337(6208):615-20 (1989).	
		PATICK, et al., "Antiviral and resistance studies of AG1343, an orally bioavailable inhibitor of human immunodeficiency virus protease," <i>Antimicrob. Agents Chemother.</i> 40(2):292-7 (1996).	
		PENG, et al., "Role of human immunodeficiency virus type 1-specific protease in core protein maturation and viral infectivity," <i>J. Virol.</i> 63(6):2550-6 (1989).	
		POORMAN, et al., "A cumulative specificity model for proteases from human immunodeficiency virus types 1 and 2, inferred from statistical analysis of an extended substrate data base," <i>J. Biol. Chem.</i> 266(22):14554-61 (1991).	

Examiner's Signature	Date Considered
<i>[Signature]</i>	<i>[Signature]</i>

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

+

Please type a plus sign (+) inside this box →



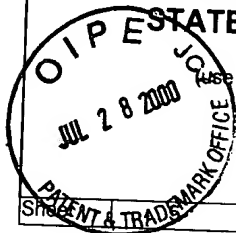
PTO/SB/08A (10-96)
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)



PATENT & TRADEMARK OFFICE

of

6

Complete if Known

Application Number

09/506,988

Filing Date

February 18, 2000

First Named Inventor

Jordan J.N. Tang

Group Art Unit

1614

Examiner Name

Attorney Docket Number

OMRF 176

OTHER ART - NON PATENT LITERATURE DOCUMENTS

Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
JMY		RIDKY & LEIS, "Development of drug resistance to HIV-1 protease inhibitors," <i>J. Biol. Chem.</i> 270(50):29621-3 (1995).	
		RIDKY, et al., "Human immunodeficiency virus, type 1 protease substrate specificity is limited by interactions between substrate amino acids bound in adjacent enzyme subsites," <i>J. Biol. Chem.</i> 271:4709-4717 (1996).	
		ROCHEFORT, "Biological and clinical significance of cathepsin D in breast cancer," <i>Semin. Cancer Biol.</i> 1(2):153-60 (1990).	
		ROSE, et al., "Human immunodeficiency virus type 1 viral background plays a major role in development of resistance to protease inhibitors," <i>Proc. Natl. Acad. Sci. USA</i> 93(4):1648-53 (1996).	
		SCHNEIDER & KENT, "Enzymatic activity of a synthetic 99 residue protein corresponding to the putative HIV-1 protease," <i>Cell</i> 54(3):363-8 (1988).	
		SIMAN, et al., "Processing of the beta-amyloid precursor. Multiple proteases generate and degrade potentially amyloidogenic fragments," <i>J. Biol. Chem.</i> 268(22):16602-9 (1993).	
		SZELKE, "Chemistry of Renin Inhibitors," in, <i>Aspartic Proteinases and Their Inhibitors</i> , (Kostka, ed.), pp. 421-441, (Walter de Gruyter:N.Y., 1985).	
		TANG & HARTSUCK, "A kinetic model for comparing proteolytic processing activity and inhibitor resistance potential of mutant HIV-1 proteases," <i>FEBS Lett.</i> 367(2):112-6 (1995).	
		TOH, et al., "Is the AIDS virus recombinant?" <i>Nature</i> 316(6023):21-2 (1985).	
JMY		TOMASSELLI, et al., "The complexities of AIDS: An assessment of the HIV protease as a therapeutic target," <i>Chimicaoggi-Chemistry Today</i> 9:6-27 (1991).	

Examiner's Signature

JMY

Date Considered

7 Sep 2000

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

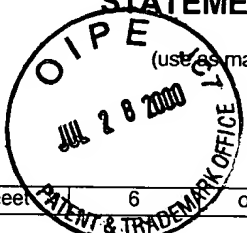
Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

Please type a plus sign (+) inside this box →

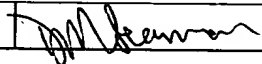


PTO/SB/08A (10-96)
Approved for use through 10/31/99. OMB 0651-0031
Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary) 		Application Number	09/506,988
		Filing Date	February 18, 2000
		First Named Inventor	Jordan J.N. Tang
		Group Art Unit	1614
		Examiner Name	
Sheet 6 of 6	Attorney Docket Number	OMRF 176	

OTHER ART – NON PATENT LITERATURE DOCUMENTS			
Examiner's Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T ²
dm		TONG, et al., "Crystal structure of human immunodeficiency virus (HIV) type 2 protease in complex with a reduced amide inhibitor and comparison with HIV-1 protease structures," <i>Proc. Natl. Acad. Sci. USA</i> 90(18):8387-91 (1993).	
		TOWLER, et al., "Functional characterization of the protease of human endogenous retrovirus, K10: can it complement HIV-1 protease?" <i>Biochemistry</i> 37(49):17137-44 (1998).	
		VACCA, "Design of Tight-Binding Human Immunodeficiency Virus Type 1 Protease Inhibitors," <i>Methods in Enzymology</i> 241:311-334 (1994).	
		WEI, et al., "Viral dynamics in human immunodeficiency virus type 1 infection," <i>Nature</i> 373(6510):117-22 (1995).	
		WEISS, et al., <i>RNA Tumor Viruses</i> , Cold Spring Harbor:NY, 1984.	
		WLODAWER & ERICKSON, "Structure-based inhibitors of HIV-1 protease," <i>Annu. Rev. Biochem.</i> 62:543-85 (1993).	
dm		WLODAWER, et al., "Conserved folding in retroviral proteases: crystal structure of a synthetic HIV-1 protease," <i>Science</i> 245(4918):616-21 (1989).	

Examiner's Signature		Date Considered	7 Sept 00
----------------------	---	-----------------	-----------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you require to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.